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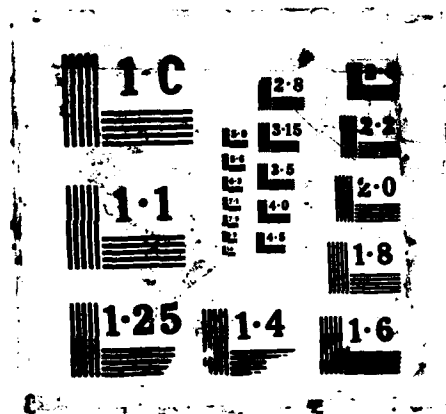
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WITH CONTROLS

by

A.S. Hedayat*, Mike Jacroux, and
Dibyen Majumdar*

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UNIVERSITY OF ILLINOIS AT CHICAGO AND
WASHINGTON STATE UNIVERSITY

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**Recent Discoveries on Optimal Designs for Comparing
Test Treatments with Controls**

by

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**University of Illinois at Chicago and
Washington State University**



ABSTRACT

This paper outlines existing knowledge on optimal designs for comparing test treatments with controls under 0-, 1-, and 2-way elimination of heterogeneity models. The results are motivated through numerical examples.

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The authors

1. Introduction. ~~We would like to~~ introduce the problem with an example. How should we design an experiment to compare 4 test treatments with a control, using 18 experimental units? As a statistical question we will not be able to answer it unless it is asked in a more precise manner. To begin with we need to postulate a model for the response observed upon application of a treatment, test treatment or control, to an experimental unit. ~~In this paper~~ we shall consider three possible models:

- 1) 0-way elimination of heterogeneity model in which all experimental units are homogeneous before application of treatments;

$$y_{ij} = \mu + t_i + \epsilon_{ij} \quad (1.1)$$

- 2) 1-way elimination of heterogeneity model in which experimental units can be divided into several homogeneous blocks; and

$$y_{ij} = \mu + t_i + \beta_j + \epsilon_{ij} \quad (1.2)$$

- 3) 2-way elimination of heterogeneity model in which the experimental units can be conceptually arranged according to rows and columns:

$$y_{ijk} = \mu + t_i + \beta_j + \rho_k + \epsilon_{ijk} \quad (1.3)$$

Now we can be more precise about what we mean by comparing test treatments with a control. Our goal is to estimate the magnitude of each $(t_i - t_0)$. Assuming that the error component ϵ in the model is homoscedastic, the method of least squares will be used to estimate the

contrasts $(t_1 - t_0)$; this happens to be the best linear unbiased estimator $(\hat{t}_1 - \hat{t}_0)$. In assigning the treatments to experimental units we have to make sure that the contrasts $(t_1 - t_0)$ are estimable. In case we have more than one choice for making this assignment we want to select one which guarantees high efficiency in the sense of achieving the minimum value of

$$\sum_{i=1}^4 \text{var} (\hat{t}_i - \hat{t}_0) \quad (1.4)$$

or

$$\max_{1 \leq i \leq 4} \text{var} (\hat{t}_i - \hat{t}_0). \quad (1.5)$$

A design which gives the minimum in (1.4) will be called an A-optimal design and one which gives the minimum in (1.5) will be called an MV-optimal design.

Without further ado we give designs which are A- and MV-optimal under each of the three models:

A- and MV-optimal design under model (1.1):

Assign 3 experimental units to each of the 4 test treatments and 6 to the control.

A- and MV-optimal design under model (1.2), when there are 6 blocks of size 3 each:

Take each column of the following array as a block:

0	0	0	0	0	0
1	1	1	2	2	3
2	3	4	3	4	4

Here 0 denotes the control and 1, 2, 3 and 4 the test treatments.

A- and MV-optimal design under model (1.3), where there are 3 rows and 6 columns:

Assign the treatments according to the following array:

1	0	3	4	2	0
0	3	4	2	0	1
4	2	0	0	1	3.

This small example demonstrates the fact that the problem of finding an optimal design is a difficult one. During the past several years there has been a concentrated effort to identify and construct optimal designs for the general problem of comparing v test treatments with a control. While in these statistical settings A- and MV-optimality are the two most natural optimality criteria, we may want to consider other optimality criteria as well in certain situations. However, in our view the published literature on other optimality criteria has not reached a level of generality for summarization. In this paper we shall attempt to summarize results on A- and MV-optimal designs, which we hope will be useful to both the theoretician and the practitioner.

In Sections 2 and 3 we give general results for A- and MV-optimal designs for comparing v test treatments with a control in each of the 3 models (1.1), (1.2) and (1.3). In Section 4 we give model robust A- and MV-optimal designs. In Section 5 we suggest various approaches for finding efficient designs in those cases where A- and MV-optimal designs are unknown. In Section 6 we give A- and MV-optimal designs for comparing test treatments with two or more controls. In Section 7 we give an overview of the literature of optimal designs for comparing test treatments with controls.

2. A-optimal Designs. We shall give A-optimal designs for comparing v test treatments with a control separately for the 0-way, 1-way, and 2-way elimination of heterogeneity. Throughout this section the control will be denoted by the symbol 0 and the test treatments by 1, 2, . . . , v .

2.0. A-optimal designs for 0-way elimination of heterogeneity. Our statistical set-up consists of n experimental units, and our model of response under a design d is

$$y_{dij} = \mu + t_i + \epsilon_{ij} \quad (2.1)$$

where $j = 1, \dots, r_{di}$, $i = 0, 1, \dots, v$. Here r_{di} is the number of experimental units receiving treatment i . We assume the model to be additive and homoscedastic. The symbols in equation (2.1) have their standard meaning. The A-optimal design minimizes

$$\sum_{i=1}^v (1/r_{d0} + 1/r_{di})$$

subject to the restriction $r_{d0} + r_{d1} + \dots + r_{dv} = n$. Using elementary mathematics, it is easily seen that an A-optimal design d^* will have $|r_{d^*i} - r_{d^*j}| \leq 1$ for $i, j = 1, \dots, v$ and

$$n - v(\bar{r}_0 + 2) \leq r_{d^*0} \leq n - v(\bar{r}_0 - 1) \quad (2.2)$$

where

$$\bar{r}_0 = \{[(2nv + v - v^2) - (v^4 + v^2 - 2v^3 + 4n^2v)^{1/2}]/2v(v-1)\} + 1. \quad (2.3)$$

Here $[x]$ denotes the integer part of the decimal expansion for $x > 0$. In the case v is a square and $n = m(v + v^{1/2})$ for an integer m , the A-optimal design d^* is:

$$r_{d^*1} = \dots = r_{d^*v} = m, \quad r_{d^*0} = m v^{1/2}.$$

2.1. A-optimal designs for 1-way elimination of heterogeneity. Our statistical set-up consists of b blocks of size k each, and the model of response under a design d is:

$$y_{dijp} = \mu + \tau_i + \beta_j + \epsilon_{ijp},$$

where $i = 0, 1, \dots, v$; $j = 1, \dots, b$ and $p = 0, 1, \dots, n_{dij}$. Here n_{dij} is the number of times treatment i is used in block j . Let N_d denote the matrix (n_{dij}) ,

$$r_{di} = \sum_{j=1}^b n_{dij},$$

$$C_d = \text{Diag} (r_{d0}, r_{d1}, \dots, r_{dv}) - k^{-1} N_d N_d',$$

$$P = \begin{pmatrix} 1 & -1 & 0 & \dots & 0 \\ 1 & 0 & -1 & \dots & 0 \\ \vdots & & & & \\ 1 & 0 & 0 & \dots & -1 \end{pmatrix},$$

P being a $v \times (v + 1)$ matrix. Then an A-optimal design minimizes

$$\text{trace } P C_d^{-} P' \quad (2.4)$$

over all possible designs, where C_d^{-} is a generalized inverse of C_d .

Experience has shown that this minimization is a difficult task. As in other cases of exact design theory, it is highly unlikely that we can obtain one method which is capable of producing A-optimal designs for arbitrary values of v , b and k . Recently several families of A-optimal designs have been discovered.

At this point it is useful to recall a celebrated result. If there was no control and if we were interested in comparing v test treatments among themselves then a BIB design in the v test treatments would be A-optimal. Unfortunately, with the presence of the control and for the set of contrasts of interest a BIB design is almost never an A-optimal design. However, we can sometimes utilize BIB designs in the test treatments to construct an A-optimal design for our problem. We shall give some families of such designs below. For convenience, we introduce the notation ABIB $(v, b, k-t; t)$ to denote a BIB design in the v test treatments in b blocks of size $k-t$ each augmented by t replications of the control in each block.

Family 1. An ABIB $(v, b, k-1; 1)$ is A-optimal whenever $(k-2)^2 + 1 \leq v \leq (k-1)^2$.

An example of an A-optimal design when $v = 7$, $b = 7$, $k = 4$ is given below, where the columns are the blocks:

0	0	0	0	0	0	0
1	2	3	4	5	6	7
2	3	4	5	6	7	1
4	5	6	7	1	2	3

For each (v, k) satisfying $(k-2)^2 + 1 \leq v \leq (k-1)^2$, there are an infinite number of A-optimal ABIB $(v, b, k-1; 1)$ designs. These results and more details are available in Hedayat and Majumdar (1985a).

Stufken (1986) has generalized the preceding idea to:

Family 2. An ABIB $(v, b, k-t; t)$ is A-optimal whenever $(k-t-1)^2 + 1 \leq t^2 v \leq (k-t)^2$.

An example of an A-optimal design when $v = 8$, $b = 28$, $k = 8$ is given below:

```

0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
3 2 2 2 2 2 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
4 4 3 3 3 3 3 4 3 3 3 3 3 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
5 5 5 4 4 4 4 5 5 4 4 4 4 5 4 4 4 4 3 3 3 3 3 3 3 3 3 3
6 6 6 6 5 5 5 6 6 6 5 5 5 6 6 5 5 5 6 5 5 5 4 4 4 4 4 4
7 7 7 7 7 6 6 7 7 7 7 6 6 7 7 7 6 6 7 7 6 6 7 6 6 5 5 5
8 8 8 8 8 8 7 8 8 8 8 8 7 8 8 8 8 7 8 8 8 7 8 8 7 8 7 6

```

Sometimes we can use two BIB designs to construct an A-optimal design for our problem. We give below one such family, which is taken from Cheng, Majumdar, Stufken and Ture (1986):

Family 3. For $v = \alpha^2 - 1$, $b = \gamma(\alpha + 2)(\alpha^2 - 1)$ and $k = \alpha$, the union of an ABIB($v, \gamma(\alpha + 1)(\alpha^2 - 1), \alpha - 1; 1$) and a BIB design in all the $v + 1$ treatments, test treatments and control, in $\gamma\alpha(\alpha + 1)$ blocks of size k each is A-optimal whenever α is a prime power, and γ is any integer.

An example when $\alpha = 3$, $\gamma = 1$, $v = 8$, $b = 40$, $k = 3$ is:

```

0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
1 1 1 1 1 1 1 2 2 2 2 2 2 3 3 3 3 3 4 4 4 4 4 4 4 4
2 3 4 5 6 7 8 3 4 5 6 7 8 4 5 6 7 8 5 6 6 6 6 6 6 6
0 0 0 0 0 0 0 0 1 4 7 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3
4 4 5 5 5 6 6 7 2 5 8 4 5 6 5 6 4 6 4 6 4 5 5 5 5 5
7 8 6 7 8 7 8 8 3 6 0 7 8 0 0 7 8 8 0 7 8 8 0 7 8 8

```

Stufken (1986b) has some more families of A-optimal designs.

To establish the optimality of these families, the starting point is a result due to Majumdar and Notz (1983), which we now proceed to state. There are many parameter combinations (v, b, k) which do not belong to any of the three families but for which Majumdar and Notz's result could still be used to get an optimal design. A complete list of all designs available by this result, when $2 \leq k \leq 8$, $k \leq v \leq 30$, $v \leq b \leq 50$ is given in Hedayat and Majumdar (1984). Before stating the result we need some definitions.

Definition 2.1. d is a Balanced Treatment Incomplete Block (BTIB) design if

$$\lambda_{d01} = \dots = \lambda_{d0v},$$

$$\lambda_{d12} = \dots = \lambda_{dv-1,v}$$

where $\lambda_{dij} = \sum_{p=1}^b n_{dip} n_{djp}$. This definition is due to Bechhofer and Tamhane (1981).

Definition 2.2. For integers $t \in \{0, 1, \dots, k-1\}$ and $s \in \{0, 1, \dots, b-1\}$, d is a $BTIB(v, b, k; t, s)$ if it is a BTIB design with the additional property that

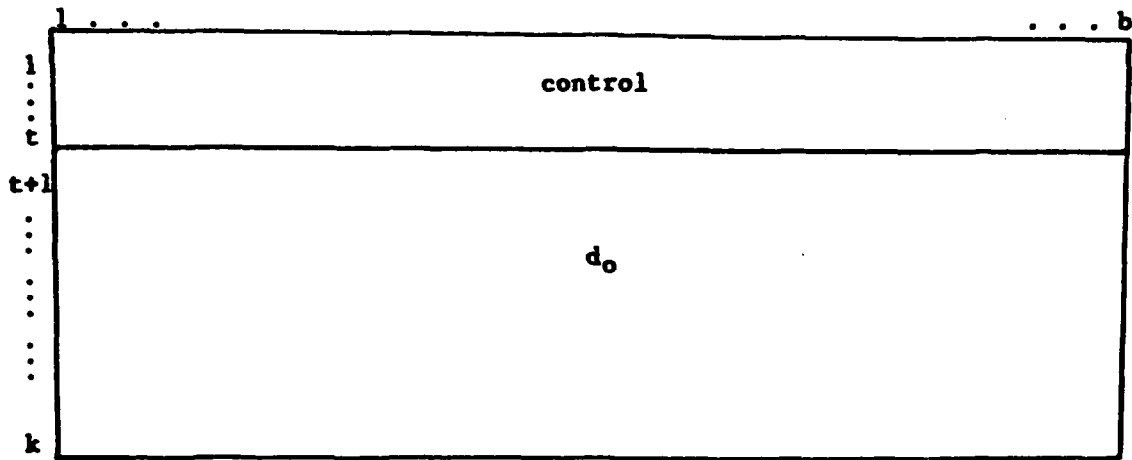
$$n_{dij} \in \{0, 1\}, \quad i = 1, \dots, v; \quad j = 1, \dots, b,$$

$$n_{d01} = \dots = n_{d0s} = t + 1,$$

$$n_{d0,s+1} = \dots = n_{d0b} = t.$$

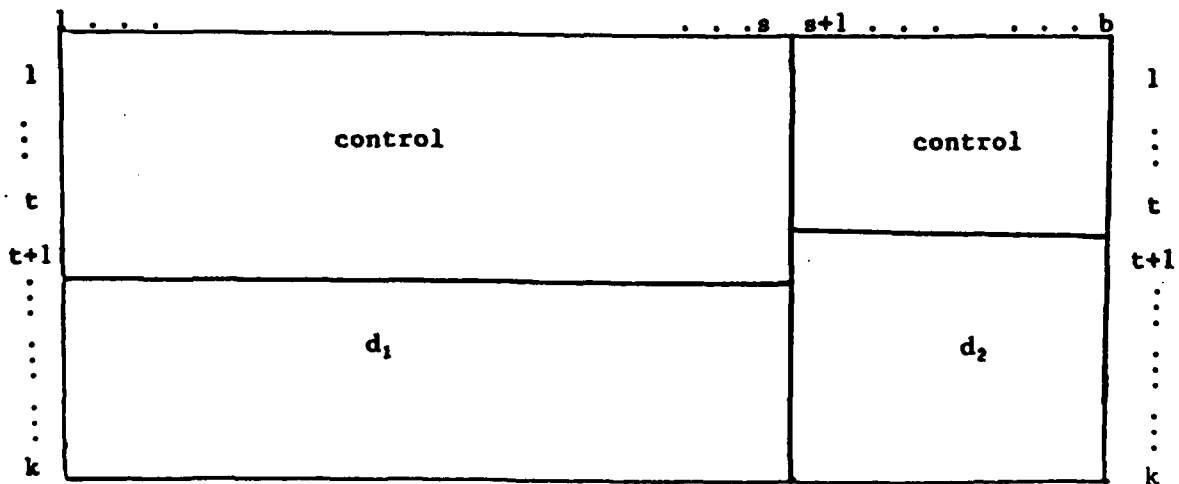
A $BTIB(v, b, k; t, s)$ is called a Rectangular (R-) type design when $s = 0$, and a Step (S-) type design when $s > 0$. The layout of these designs can be pictured as follows, with columns as blocks, in each of the two cases R-type and S-type:

(i) R-type



d_0 is a BIB design in the test treatments.

(ii) S-type.



d_1 and d_2 are components of the design which involve the test treatments only.

We shall also need the following notations:

$$\Lambda = \{(x,z): x=0, \dots, [k/2]-1; z=0, \dots, b \text{ with } z>0 \text{ when } x=0\} \quad (2.5)$$

$$a = (v-1)^2, c = bvk(k-1), p = v(k-1) + k$$

$$A(x,z) = \{c - p(bx+z) + bx^2 + 2xz + z\} / vk$$

$$B(x,z) = \{k(bx+z) - (bx^2 + 2xz + z)\} / vk$$

$$g(x,z) = a/A(x,z) + 1/B(x,z).$$

Now we are ready to state the result of Majumdar and Notz (1983).

Theorem 2.1. Let v, b, k be integers with $k \leq v$. A BTIB($v, b, k; t, s$) is A-optimal in the class of all designs if

$$g(t, s) = \text{Min } \{g(x, z) : (x, z) \in \Lambda\}.$$

Hedayat and Majumdar (1984) have devised an algorithm for obtaining A-optimal designs based on Theorem 2.1. Jacroux (1986) has generalized this algorithm. His algorithm is often capable of producing A-optimal designs which are not necessarily BTIB in their structure. In particular, the algorithm given by Jacroux (1986) often produces A-optimal group divisible treatment designs (GDTD's).

Definition 2.3. d is a GDTD with parameters $m, n, \lambda_0, \lambda_1$ and λ_2 if the treatments $1, \dots, v$ can be divided into m groups V_1, \dots, V_m of size n such that

- (i) $\lambda_{doi} = \lambda_0$ for $i = 1, \dots, v$ and for some constant λ_0 ,
- (ii) if $i, j \in V_p, i \neq j$, $\lambda_{dij} = \lambda_1$ for some constant λ_1 ,
- (iii) if $i \in V_p, j \in V_q, p \neq q$, $\lambda_{dij} = \lambda_2$ for some constant λ_2 .

Definition 2.4. For integers $t \in \{0, 1, \dots, k-1\}$ and $s \in \{0, 1, \dots, b-1\}$, d is a $\text{GDTD}(v, b, k; t, s)$ if it is a GDTD with the additional property that

$$n_{di,j} \in \{0, 1\}, \quad i = 1, \dots, v, j = 1, \dots, b,$$

$$n_{ds,1} = \dots = n_{ds,b} = t + 1,$$

$$n_{do,s+1} = \dots = n_{dob} = t.$$

A $\text{GDTD}(v, b, k; t, s)$ is called an R -type design when $s = 0$ and an S -type design when $s > 0$.

To state Jacroux's generalization of Theorem 2.1, we will let a, c, p $A(x, z)$, $B(x, z)$, and $g(x, z)$ be as defined in (2.5) and also introduce the following notations:

$$\bar{A} = \{(x, z): x = 0, \dots, k-2; z = 0, \dots, b \text{ with } z > 0 \text{ when } x = 0\} \quad (2.6)$$

$$R(x, z) = [(bk - bx - z)/v].$$

$$\lambda(x, z) = [(bk - bx - z)(k-1) - vkB(x, z)]/v(v-1)$$

$$\begin{aligned} C(x, z) = & \{bk - bx - z - vR(x, z)\} \{R(x, z)(k-1)\}^2 / k^2 \\ & + \{(v - bk + bx + z + vR(x, z)) \{R(x, z)(k-1)\}^2 / k^2 + \{A(x, z) - v(v-1)\lambda(x, z)\} \{\lambda(x, z) \\ & + 1\}^2 / k^2 + \{v(v-1) - A(x, z) + v(v-1)\lambda(x, z)\} \lambda^2(x, z) / k^2. \end{aligned}$$

$$i(x, z) = \{C(x, z) - B^2(x, z) - A^2(x, z)/(v-1)\}^{\frac{1}{2}}$$

$$h(x, z) = a/(A(x, z) - 2/k) + 1/B(x, z).$$

$$m(x, z) = \begin{cases} g(x, z) & \text{if } B(x, z) > \{A(x, z) - ((v-1)/(v-2))^{\frac{1}{2}} P(x, z)\} / (v-1), \\ 1/B(x, z) + (v-2)(v-1) / \{A(x, z) - ((v-1)/(v-2))^{\frac{1}{2}} P(x, z)\} \\ + (v-1) / \{A(x, z) + ((v-1)(v-2))^{\frac{1}{2}} P(x, z)\}, & \text{otherwise} \end{cases}$$

$$n(x, z) = \min \{h(x, z), m(x, z)\}.$$

Theorem 2.2. Let v, b, k be integers with $k \leq v$. A $\text{BTIB}(v, b, k; \bar{t}, \bar{s})$ or a $\text{GDTD}(v, b, k; \bar{t}, \bar{s})$ having $m = 2$, $n = v/2$ and $\lambda_2 = \lambda_1 + 1$ is A -optimal in the class of all designs if

$$n(\bar{t}, \bar{s}) = \min \{n(x, z) : (x, z) \in \bar{A}\}.$$

We note that many BTIB($v, b, k; \bar{t}, \bar{s}$) designs not satisfying the conditions of Theorem 2.1 can be shown to satisfy the conditions of Theorem 2.2. In addition, Theorem 2.2 can be used to establish the A-optimality of GDTD($v, b, k; \bar{t}, \bar{s}$)'s having $m = 2$, $n = v/2$ and $\lambda_2 = \lambda_1 + 1$. Using some more elaborate computational techniques, Jacroux (1986) has also developed some sufficient conditions for GDTD($v, b, k; \bar{t}, \bar{s}$)'s having $\lambda_2 = \lambda_1 + 1$ or $m = v/2$, $n = 2$ and $\lambda_2 = \lambda_1 - 1$ to be A-optimal among all designs with parameters v , b , and k . One example of an A-optimal GDTD is that GDTD(9,9,4;1,0) d^* having $m = 3$, $n = 3$, $\lambda_1 = 0$ and $\lambda_2 = 1$ given below:

0	0	0	0	0	0	0	0	0
1	1	1	2	2	2	3	3	3
4	5	6	4	5	6	4	5	6
7	8	9	8	9	7	9	7	8

2.2. A-optimal designs for 2-way elimination of heterogeneity. Our statistical setup consists of bk experimental units arranged in a $k \times b$ array, and the model of response under design d is:

$$y_{dij\lambda} = \mu + \tau_i + \beta_j + \rho_\lambda + \epsilon_{ij\lambda} \quad (2.7)$$

($i = 0, 1, \dots, v$; $j = 1, \dots, b$; $\lambda = 1, \dots, k$) if treatment i is applied to the experimental unit in cell (j, λ) .

Let

n_{dij} = number of times treatment i occurs in column j ,

$m_{di\lambda}$ = number of times treatment i occurs in row λ ,

$$r_{di} = \sum_{j=1}^b n_{dij},$$

$N_d = (n_{dij})$, a $v \times b$ matrix,

$M_d = (m_{di\lambda})$, a $v \times k$ matrix,

P is the $v \times (v + 1)$ matrix defined in subsection 2.1,

$$r_d = (r_{d0}, r_{d1}, \dots, r_{dv})',$$

$$C_d(z) = (r_{d0}, r_{d1}, \dots, r_{dv}) - k^{-1} M_d M_d' - b^{-1} M_d M_d' + (bk)^{-1} r_d r_d'.$$

Then an A-optimal design minimizes trace $PC_{d(z)}^{-1}P'$. We shall now highlight some of the results from recent literature.

Family 1. Let p be an integer and $v = p^2$, $b = k = p^2 + p$. A $b \times b$ array in which each test treatment appears once in each row and in each column and the control appears p times in each row and in each column is A-optimal.

One easy way to construct members of this family is to start with a Latin square of order $p^2 + p$ and change symbols $p^2 + 1, \dots, p^2 + p$ to 0 (control). We illustrate this in the following example with $v = 4$, $b = k = 6$.

1	2	3	4	5	6		1	2	3	4	0	0
6	1	2	3	4	5		0	1	2	3	4	0
5	6	1	2	3	4	→	0	0	1	2	3	4
4	5	6	1	2	3		4	0	0	1	2	3
3	4	5	6	1	2		3	4	0	0	1	2
2	3	4	5	6	1		2	3	4	0	0	1

This and some more general results are available in Notz (1985).

This has been generalized by Majumdar (1986).

Family 2. Let p , α and γ be integers, $v = p^2$, $k = \alpha(p^2 + p)$ and $b = \gamma(p^2 + p)$. A $k \times b$ array in which each test treatment appears α times in each column and γ times in each row, and the control appears αp times in each column and γp times in each row is A-optimal.

One way to construct members of this family is to form the array

$$(L_{ij}), i = 1, \dots, \alpha; j = 1, \dots, \gamma$$

where each L_{ij} is a member of Family 1.

Family 3. A $k \times b$ array is A-optimal if

- (i) it is an A-optimal block design for 1-way elimination of heterogeneity with columns as blocks, and
- (ii) the total number of replications for each treatment, test treatment or control, is divided equally among the k rows.

This has been given by Jacroux (1984c). The following is an example when $v = 9$, $b = 24$, $k = 3$:

0	4	1	0	2	5	7	8	3	0	9	6	0	0	8	0	7	9	1	6	2	3	4	5
1	0	5	8	0	2	0	0	5	2	0	4	4	6	6	9	0	7	2	1	3	8	7	9
3	1	0	1	4	0	2	2	0	7	3	0	9	5	0	6	8	0	9	7	6	4	5	8

3. MV-optimal Designs. In this section we give a number of results concerning the MV-optimality of designs for comparing v test treatments with a control for the 0-way, 1-way and 2-way elimination of heterogeneity. The notation introduced in Section 2 is also used throughout this section.

3.0. MV-optimal designs for 0-way elimination of heterogeneity. Our statistical setup is the same as given in Subsection 2.0. An MV-optimal design minimizes

$$\max_{1 \leq i \leq v} (1/r_{d0} + 1/r_{di}) \quad (3.1)$$

subject to the restriction $r_{d0} + r_{d1} + \dots + r_{dv} = n$. Using elementary mathematics, it is easily seen that an MV-optimal design d^* has

$$r_{d^*i} = r_{d^*0} \text{ for } i = 1, \dots, v \text{ and } r_{d^*0} = n - \sqrt{v+1}$$

where \bar{r}_0 is given in (2.3). We note that for a fixed value of n , the A- and the MV-optimality criteria may select substantially different optimal designs from those available. For example, when $n = 30$ and $v = 15$, an A-optimal design \bar{d} will have $r_{\bar{d}0} = 5$ and $r_{\bar{d}i} = 1$ or 2 for $i = 1, \dots, 15$ whereas the MV-optimal design d^* will have $r_{d^*0} = 15$ and $r_{d^*i} = 1$ for $i = 1, \dots, 15$.

3.1. MV-optimal designs for the 1-way elimination of heterogeneity. Our statistical set-up is the same as given in Subsection 2.1. We note that any design which is A-optimal among all designs having parameters v, b and k and which estimates all contrasts of the form $t_1 - t_0$ with the same variance will also be MV-optimal. Thus we see that all designs given in Subsection 2.1 as being A-optimal are also MV-optimal since all GDTD $(v, b, k; \bar{r}, \bar{s})$'s estimate contrasts of the form $t_1 - t_0$ with the same variance. However, Jacroux (1986) has developed some additional sufficient conditions which can be used to establish the MV-optimality of various GDTD $(v, b, k; x, z)$'s which cannot be proven to be A-optimal using any known results. As an example of the types of results which can be proven for MV-optimality, we have the following.

Theorem 3.1. Let d^* be a BTIB $(v, b, k; \bar{t}, \bar{s})$ where

$$n(\bar{t}, \bar{s}) = \min \{n(x, z) : (x, z) \in \bar{A}, (bk - bx - z)/v \text{ is an integer}\}$$

and for positive integers p and q , let $\bar{B}(p, q)$ denote the smallest value of y such that

$$(1, -1) \begin{pmatrix} p/k & -y/k \\ -y/k & q/k \end{pmatrix}^{-1} \begin{pmatrix} 1 \\ -1 \end{pmatrix} \leq \text{var}(\hat{t}_{d^*1} - \hat{t}_{d^*0})$$

where \hat{t}_{d^*1} is the least squares estimate of t_1 obtained under d^* .

Also let $R(x,z) = [(bk - bx - z)/v]$. If for any $(x,z) \in \bar{A}$ such that $n(x,z) < n(\bar{t}, \bar{s})$, it holds that

$$vkB(x,z) < (bk-bx-z-vR(x,z))\bar{B}(vkB(x,z), (R(x,z)+1)(k-1)) \\ + (v-bk+bx+z+vR(x,z))\bar{B}(vkB(x,z), R(x,z)(k-1)),$$

then d^* is MV-optimal among all designs.

Using some more complex computational techniques, Jacroux (1986) has obtained some further results similar to Theorem 3.1 which can be used to establish the MV-optimality of various $GTD(v,b,k;\bar{t},\bar{s})$'s having $0 \leq \lambda_2 - \lambda_1 \leq 1$ or $m = v/2$, $n = 2$ and $\lambda_2 = \lambda_1 - 1$ whose A-optimality remains unknown.

For example when $v = 6$, $b = 11$ and $k = 3$, as well as when $v = 6$, $b = 16$ and $k = 4$, an A-optimal design is unknown. However, we are able to give designs whose MV-optimality can be established using results such as Theorem 3.1. These are exhibited below:

Example 3.1. $v = 6$, $b = 11$ and $k = 3$.

0	0	0	0	0	0	0	0	0	1	4
1	1	1	2	2	2	3	3	3	2	5
4	5	6	4	5	6	4	5	6	4	6

Example 3.2. $v = 6$, $b = 16$ and $k = 4$.

0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	1	2	3	1	3	1	2	1	2	1	2	1	3	1	2
2	5	4	4	2	5	4	3	3	5	4	3	2	4	3	4
3	6	6	5	4	6	6	6	4	6	6	5	5	6	6	5.

It is interesting to note that the design in Example 3.1 is an S-type BTIB design, while the design given in Example 3.2 is a GDTD.

3.2. MV-optimal designs for the 2-way elimination of heterogeneity.

Again our statistical set-up is the same as that given in Subsection 2.2. Using arguments similar to those used in Subsection 3.1, we see that all of the A-optimal row-column designs which estimate treatment contrasts $t_1 - t_0$ with the same variance will also be MV-optimal. Thus all the A-optimal row-column designs listed in Subsection 2.2 are also MV-optimal. In addition, a $k \times b$ array is MV-optimal if

- (i) it is an MV-optimal block design for 1-way elimination of heterogeneity with columns as blocks, and
- (ii) the total number of replications for each treatment, test treatment or control, is divided equally among the k rows.

Example 3.3. For $v = 6$, $b = 16$ and $k = 4$, the row-column design given by

0	6	4	5	0	3	1	2	0	5	6	2	0	3	1	4
1	0	6	4	2	0	5	3	1	0	4	3	5	0	6	2
2	1	0	3	4	6	0	6	3	2	0	5	1	4	0	5
3	5	2	0	1	5	4	0	4	6	1	0	2	6	3	0

is MV-optimal.

4. Model Robust Optimal Designs. There are circumstances in which the experimenter is not sure whether to fit a 1-way or a 2-way elimination of heterogeneity model to the data. In such situations it would be highly desirable to obtain a design which is A- or MV-optimal under each of these

models. Hedayat and Majumdar (1986b) studied this aspect of the problem and gave some families of model robust designs. The families were constructed using the Euclidean plane, the Projective plane and some other geometrical structures. The exact description of the families are somewhat involved; some typical examples are given below.

Example 4.1. Let $v = 4$, $k = 3$ and $b = 6$. The following design is A- and MV-optimal for both 1- and 2-way elimination of heterogeneity models:

1	0	3	4	2	0
0	3	4	2	0	1
4	2	0	0	1	3

In fact, this design is A- and MV-optimal for the 0-way elimination of heterogeneity model as well.

Example 4.2. Let $v = 7$, $k = 4$ and $b = 28$. The following design is A- and MV-optimal for both 1- and 2-way elimination of heterogeneity models:

0 0 0 0 0 0 0	1 2 3 4 5 6 7	1 2 3 4 5 6 7	1 2 3 4 5 6 7
1 2 3 4 5 6 7	0 0 0 0 0 0 0	2 3 4 5 6 7 1	2 3 4 5 6 7 1
2 3 4 5 6 7 1	2 3 4 5 6 7 1	0 0 0 0 0 0 0	4 5 6 7 1 2 3
4 5 6 7 1 2 3	4 5 6 7 1 2 3	4 5 6 7 1 2 3	0 0 0 0 0 0 0

Before closing this section we would like to mention that the designs in families 1 and 2 in subsection 2.2 are A- and MV-optimal under 0-way, 1-way and 2-way elimination of heterogeneity models, while the designs in family 3 are A- and MV-optimal at least under 1-way and 2-way elimination of heterogeneity models.

5. Other Efficient Designs. Even though, for each set of v test treatment there is an A- or MV-optimal design for a 0-, 1- or 2-way elimination of heterogeneity model, the task of finding this design can be very difficult indeed. For situations where an A- or MV-optimal design is unknown, there are several alternative ways of planning an experiment. Here are some possibilities.

5.1. Limit the class of competing designs to a "reasonably rich" subclass, so that an A- or MV-optimal design within this subclass can be constructed. For example, under a 1-way elimination of heterogeneity model the BTIB designs form such a subclass. For $v = 3$, $b = 15$, $k = 2$ the A- or MV-optimal design is not available in the literature, but a design which is A- and MV-optimal among all BTIB designs is given by

0	0	0	0	0	0	0	0	0	1	1	2
1	1	1	2	2	2	3	3	3	2	3	3

This approach has been studied in Hedayat and Majumdar (1984) under the A-optimality criterion, and some series of such designs have been cataloged. Numerical evidence indicates that optimal designs obtained in this fashion are highly efficient in the class of all designs. There are, however, isolated instances where they perform poorly. A similar study for the MV-optimality criterion has been carried out by Jacroux (1985).

5.2. Search for an approximately A- or MV-optimal design. This can be carried out in two steps. First compute

$$(i) \quad g(t,s) = \text{Min}\{g(x,z):(x,z) \in \Lambda\}$$

or

(5.1)

$$(ii) \quad g(t,s)/v = \text{Min}\{g(x,z):(x,z) \in \Lambda\}/v$$

where the function $g(x,z)$ has been defined in Subsection 2.1. These give lower bounds to the values of the A- and MV-criterion, respectively. The second step consists of guessing a good design \bar{d} based on available theory. Compute the corresponding value of the expression (2.4) or $\max_{1 \leq i \leq v} \text{var}(\hat{t}_{d1} - \hat{t}_{d0})$ for this design and compare with the appropriate minimum value given in (5.1). If the comparison is poor in the opinion of the experimenter, then he should modify his guess and try again.

Let us demonstrate this approach by an example. Let $v = 21$, $b = 30$ and $k = 9$. Here the minimum given by (5.1(i)) is 2.589 and that given by (5.1(ii)) is .1233. Our experience shows that BIB designs in the test treatments augmented by one or more replications of the control in each block are often highly efficient, as seen in families 1 and 2 of Subsection 2.1. In our case we can try a design, \bar{d} , which is an ABIB(21,30,7;2).

For this design the value of (2.4) is 2.618 and $\max_{1 \leq i \leq v} \text{var}(\hat{t}_{\bar{d}1} - \hat{t}_{\bar{d}0}) = .1247$, giving an efficiency of at least 98.87% for both the A- and MV-optimality criteria. So this is indeed a highly efficient design. This approach of approximating an A- and MV-optimal design by an augmented BIB design has been studied by Stufken (1986c).

Another method of tracking down a good approximation has been given in Cheng, Majumdar, Stufken and Ture (1986). It consists of first determining the point (t,s) which minimizes the function $g(x,z)$ given in (5.1). In case a BTIB($v,b,k;t,s$) exists, it is both A- and MV-optimal. If it does not, then at least one of the following two designs is expected to be a good approximation:

- (i) A design with the same number $(bt+s)$ of replications of the control as a BTIB($v,b,k;t,s$) and which is "combinatorially close" to a BTIB design.

(ii) A BTIB design with the number of replications of the control "close" to $bt + s$.

We demonstrate the idea by an example when $v = 5$, $b = 7$ and $k = 4$. Here $(t,s) = (1,0)$ and $g(t,s) = 2.04$. There is no BTIB(5,7,4;1,0). Consider the following two designs:

	0	0	0	0	0	0	0		0	0	0	0	0	0	1
	1	1	1	1	1	2	2		0	0	1	1	2	2	2
$d_1 :$	2	2	3	3	4	3	3	$d_2 :$	1	3	3	4	3	4	3
	4	5	4	5	5	4	5		2	4	5	5	5	5	4

Here $bt + s = 7$, d_1 is a non-BTIB design with 7 replications of the control, while d_2 is a BTIB design with 8 replications of the control. The value for expression (2.4) for d_1 is 2.058 giving it an efficiency of 99.2%. The value for expression (2.4) for d_2 is 2.143 giving it an efficiency of 95.2%. Thus both of these designs are highly efficient under the A-criterion, d_1 being the better of the two.

Finally, with the availability of today's high-speed computers and supercomputers, one can find an A- or MV-optimal design by a complete search among all possible designs if the parameters v , b and k are not too large.

6. A- and MV-optimal Designs for Two or More Controls. So far we have been discussing optimal designs for comparing test treatments with one control. There are circumstances when the test treatments have to be compared with two or more controls. Suppose we denote by S the set of all controls and by T the set of all test treatments. Then, an A-optimal design is the one which minimizes

$$\sum_{g \in S} \sum_{h \in T} \text{var}(\hat{t}_{dg} - \hat{t}_{dh}),$$

and an MV-optimal design is one which minimizes

$$\max_{g \in S, h \in T} \text{var}(\hat{t}_{dg} - \hat{t}_{dh})$$

among all designs under a 0-way, 1-way or 2-way elimination of heterogeneity model. Majumdar (1986) has studied this problem, and has identified designs which are A- and MV-optimal in various settings. Here we give an example of an A- and MV-optimal design for one way elimination of heterogeneity and an example of a design which is optimal for each of 0-, 1- and 2-way elimination of heterogeneity.

Example 6.1. Suppose 4 test treatments are to be compared with 3 controls in 30 blocks of size 3 each under the 1-way elimination of heterogeneity model. Denoting the test treatments by A,B,C,D and the controls by 1, 2, and 3 the A- and MV-optimal design is:

1	1	2	1	1	2	1	1	2	1	1	2	1	1	1	1	1	
2	3	3	2	3	3	2	3	3	2	3	3	A	A	A	B	B	C
A	A	A	B	B	B	C	C	C	D	D	D	B	C	D	C	D	D

2	2	2	2	2	2	3	3	3	3	3	3
A	A	A	B	B	C	A	A	A	B	B	C
B	C	D	C	D	D	B	C	D	C	D	D

Example 6.2. Suppose 8 test treatments are to be compared with 2 controls in a 12 x 12 array under a 2-way elimination of heterogeneity model. Denoting the test treatments by A,B,C,D,E,F,G,H, and the controls by 1,2, the A- and MV-optimal design is given by

A	B	C	D	E	F	G	H	1	1	2	2
B	C	D	E	F	G	H	1	1	2	2	A
C	D	E	F	G	H	1	1	2	2	A	B
D	E	F	G	H	1	1	2	2	A	B	C
E	F	G	H	1	1	2	2	A	B	C	D
F	G	H	1	1	2	2	A	B	C	D	E
G	H	1	1	2	2	A	B	C	D	E	F
H	1	1	2	2	A	B	C	D	E	F	G
1	1	2	2	A	B	C	D	E	F	G	H
1	2	2	A	B	C	D	E	F	G	H	1
2	2	A	B	C	D	E	F	G	H	1	1
2	A	B	C	D	E	F	G	H	1	1	2

This design is model robust in the sense of being A- and MV-optimal for 0- and 1-way elimination of heterogeneity models as well.

7. Discussion. Cox (1958, p.238) advocated augmenting a BIB design in test treatments with one or more replications of controls in each block as a means of getting good designs. He neither formally mathematized the problem nor gave any justification for his suggestion. However, based on what has been developed during the past several years, we know that this is an excellent method of getting efficient designs in many cases. Pearce (1960) gave a solution for A-optimal designs for the 0-way elimination of heterogeneity model which is applicable when v is a square, and proposed a class of designs for comparing test treatments with a control and gave their analysis for the 1-way elimination of heterogeneity model. Freeman (1975) studied some designs for comparing two sets of treatments for the 2-way elimination of heterogeneity model. Pesek (1974) compared a BIB

design with an augmented BIB design, as suggested by Cox (1958), in estimating control-test treatment contrasts and noticed that the latter was more efficient. Das (1958) has also looked at augmented BIB designs.

Bechhofer and Tamhane (1981) were the first to study the problem of obtaining optimal block designs. However their optimality consideration was neither A- nor MV-optimality, but for the problem of obtaining optimal simultaneous confidence intervals under a 1-way elimination of heterogeneity model. Their discoveries led to the concept of BTIB designs; Notz and Tamhane (1983) studied their construction.

Constantine (1983) showed that a BIB design in test treatments augmented by a replication of the control in each block is A-optimal in the class of designs with exactly one replication of the control in each block. Jacroux (1984a) showed that Constantine's conclusion remains valid even when the BIB designs are replaced by some group divisible designs.

Majumdar and Notz (1983) gave a method of obtaining A- and MV-optimal designs among all designs for the 1-way elimination of heterogeneity model. Hedayat and Majumdar (1984) gave an algorithm and a catalog of A- and MV-optimal designs and studied approximations. Ture (1982) also studied A-optimal designs and their approximations and construction. Hedayat and Majumdar (1985a) gave families of A- and MV-optimal designs. Notz (1985) studied optimal designs for the 2-way elimination of heterogeneity model. Majumdar (1986) considered the problem of finding optimal designs for comparing the test treatments with two or more controls.

Jacroux (1984b, 1985) gave new methods for obtaining MV-optimal designs under 1-way elimination of heterogeneity models, gave catalogs and studied approximations. Jacroux (1984c) studied optimal designs for 2-way elimination of heterogeneity models, utilizing techniques of Hall (1935)

and Agarwal (1966). Hedayat and Majumdar (1985b) studied designs simultaneously optimal under both 1- and 2-way elimination of heterogeneity models. Jacroux (1986) generalized the Hedayat and Majumdar (1984) algorithm for finding A-optimal designs. Cheng, Majumdar, Stufken and Ture (1986) gave new families of A- and MV-optimal designs and some approximations for 1-way elimination of heterogeneity models. Stufken (1986a,b,c) studied A- and MV-optimal designs for 1-way elimination of heterogeneity models, gave families and studied approximations.

There are many other design settings in which it would be useful to identify optimal designs for comparing test treatments with controls. One such setting is that of repeated measurements designs. Some aspects of optimality and construction of designs in this area has been investigated by Pigeon (1984).

Giovagnoli and Wynn (1985) studied A-optimality of designs for 1-way elimination of heterogeneity models set in the context of approximate theory, i.e. with an infinite number of observations. Spurrier and Edwards (1986) did a similar study for optimal designs for finding simultaneous confidence intervals.

It seems appropriate to make a comment on randomization. In running optimal designs we often have to follow a well structured pattern. This does not, however, mean that there will be no room for randomization. The labelling of the treatments, experimental units under a 0-way elimination of heterogeneity model, blocks under a 1-way elimination of heterogeneity model and rows and columns under a 2-way elimination of heterogeneity model can be randomized.

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